

FIG. 1

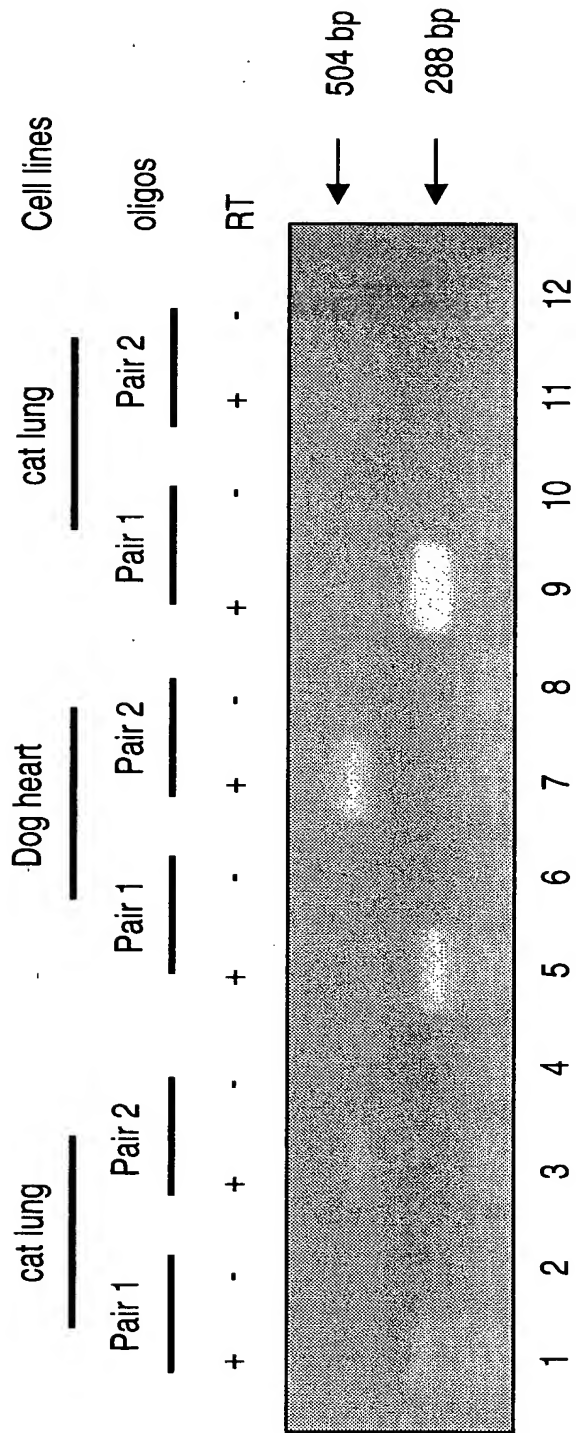


FIG. 2

GCTATACTCGGGCGCGGTACCATAACTTTCGTATAGCATAACATTATACGAAGTTAT
CGGAGGAATTGGCTCGAGGAATTGCCCTTCTAATACGACTCACTATAGGGCAAGC
AGTGGTAACAACGCAGAGTACGCGGGAGCACGGACCGGCGGGGGGCGAGCGAGATG
CAGGCCCGGGGGGGCCCCAGCCTCGGGCTGACGTGCGTGCTGATCCTCATCTTCA
CTGTGCTGCTCCAGTCCCTCTGCGTGGCCGTACCTACATGTACTTCACCAGGGA
GCTGAAGCAGATGCAGGACAAGTACTCCCAAAGTGGCATCGCTTGTTTCTTAAAG
GAAGATGATATCCCCTGGGACCCAGTGATGAAGAGAGTATGAACAACCCCTGCT
GGCAAGTGAAGTGGCAACTCCGCCAGTTTGTTAGAAAGATGATTTTGAAAACCTA
TGAGGAAACCATTCCTACAGCTCCAGAAAAGCAGCTAAATATTCTTACGTAGTA
AGCGACCGAGGTTCTCAGAGAGTAGCTGCTCACATAACTGGAACCAAGTCGGAGAA
GCATGTTTCCAATTCCAAGCTCCAAGAATGATAAAGCTTTGGGCCACAAAATAAA
CTCCTGGGATTCCACAAGAAAAGGACATTCATTCTTGAATAATTTGCACTTGAGG
AACGGAGAGCTGGTTATCCATCAAAGGGGGTTTTATTACATCTATTCCCAAACAT
ACTTTCGATTTTCAGGAACCTGAGGAAATTCCAACAGGACAGAACAGAAAGAGAAA
CAAACAAATGGTCCAATATATTTACAAACACACGAGTTATCCGGACCCTATACTG
CTGATGAAAAGTGCTAGAAATAGTTGTTGGTCTAAAGATTCTGAATATGGACTCT
ATTCCATCTATCAAGGTGGGATATTTGAGCTTAAGGAAAACGATAGAATTTTTGT
CTCTGTATCTAACGAGCAATTGATTGACATGGACCAAGAAGCCAGTTTTTTTCGGG
GCCTTTTTTAATCGGCTAAATACGCTGCAAAGAAAAAAAACGTATTCTTTATTC
ACAGCAAAGCAAGGACATCTAAGCAAAGTCACGTCAACCAAAGAGTAACACGCC
TTTCTCAAACATCTCTGAAAATGACCAAGTCATTCTCAGAAAATGAAATTGCCGA
AGACCTTTCCAGGCACTACCAAGAGATCAGTTTGCTAGCAGAAACCTAGAAGATT
CTGTAAGCAGCTGTCTTTATTATCTACTCTTGGAAGACCCAGAAGCAAGATTA

FIG. 3

MQAPGGPSLGLTCVLILIFTVLLQSLCVAVTYMYFTRELKQMQDKYSQSGIACFL
KEDDIPWDPSDEESMNNPCWQVKWQLRQFVRKMILKTYEETIPTAPEKQLNIPYV
VSDRGSRVAAHITGTSRRSMFPIPSSKNDKALGHKINSWDSTRKGHSFLNNLHL
RNGELVIHQRGFYIYSQTYFRFQEP E EIPTGQNRKRKQMVQYIYKHTSYDPDI
LLMKSARNSCWSKDSEYGLYSIQGGIFELKENDRIFVSVSNEQLIDMDQEASFF
GAFLIG

FIG. 4

GAATTGCCCTTCTAATACGACTCCCTATAGGGCAAGCAGTGGTAACAACGCAGAG
TACGCGGGGGCAGCAGTGA CTGTCGGAGAGGACAGGACCGTGGTTCGAGATGCAGG
CCCCGGCGGGCCCCAGTCCCGGGCAGACCTGCGTGCTGATCCTGATCTTCACTGT
GCTCCTGCAGTCCCTCTGCGTGGCCGTGACTTACATGTACTTCACCACTGAAGT
AGGCAGATGCAGGACAAATACTCCCAAAGTGGCATTGCTTGTTTCTTAAAGGAAG
ACGATATCCCTTGGGACCCCAATGATGAAGAGAGTATGAACACCCCGTGCTGGCA
AGTGAAATGGCAGCTCCGTCAGTTTGTTAGAAAGATTTTGAGAACCTATGAGGAA
ACCATTCCTACAGTTCCAGAAAAGCAGCTAAATATTCCTTACCTAGTAAGAGAAA
GAGGTCCTCAGAGAGTAGCAGCTCACATAACTGGAACCACTCGGAGAAGAAGCAC
ATTCCAGTTCCAAGCTCCAAGAATGAAAAAGCTTTGGGTCAGAAAATAAACTCC
TGGGAGTCATCAAGAAAAGGACATTCATTCTTGAATAATTTGCACTTGAGGAATG
GTGAGCTGGTTATTCATCAGAGGGGGTTTTATTACATCTATTCCCAAACATACTT
TCGATTTTCAGGAACCTGAGGAAATTCCAACAGGACAGAACAGAAAGAGAAACAAA
CAAATGGTCCAATATATTTACAAACACACGAGTTATCCGGACCCCTATACTGCTGA
TGAAAAGTGCTAGAAATAGTTGTTGGTCTAAAGATTCTGAATATGGACTCTATTC
CATCTATCAAGGTGGGATATTTGAGCTTAAGGAAAACGATAGAATTTTTGTCTCT
GTATCTAACGAGCAATTGATTGACATGGACCAAGAAGCCAGTTTTTTTCGGGGCCT
TTTTAATCGGCTAAATACGCTGCAAAGAAAAAAAACCTGTATTCTTTATTCACAG
CAAAGCAAGGACATCTAAGCAAAGTCACGTCAACCAAAGAGTAACACGCCTTTC
TCAAACATCTCTGAAAATGACCAAGTCATTCTCAGAAAATGAAATTGCCGAAGAC
CTTTCCAGGCACTACCAGAGATCAGTTTGCTAGCAGAAACCTAGAAGATTCTGTA
AGCAGCTG

FIG. 5

MQAPAGPSPGQTCVLILIFTVLLQSLCVAVTYMYFTSELRQMQDKYSQSGIACFL
KEDDIPWDPNDEESMNTPCWQVKWQLRQFVRKILRTYEETIPTVPEKQLNIPYLV
RERGPQ RVA AHITGTSRRRSTFPVPSSKNEKALGQKINSWESSRK GHSFLNNLHL
RNGELVIHQRGFYIYSQTYFRFQEP E EIPTGQNRKR NKQMVQYIYKHTSYDPDI
LLMK SARNSCWSKDSEYGLYSIYQGGIFELKENDRIFVSVSNEQLIDMDQEASFF
GAFLIG

FIG. 6B

		80		90			
72	Ser Met Asn Ser	Pro Cys Trp Gln Val Lys Trp Gln Leu Arg Gln	hu_Trail.PRO				
76	Ile Leu Asn Arg	Pro Cys Leu Gln Val Lys Arg Gln Leu Tyr Gln	mo_Trail.PRO				
69	Ser Met Asn Asn	Pro Cys Trp Gln Val Lys Trp Gln Leu Arg Gln	canine_Trail.PRO				
69	Ser Met Asn Thr	Pro Cys Trp Gln Val Lys Trp Gln Leu Arg Gln	feline_Trail.PRO				
		100					
87	Leu Val Arg Lys Met	Ile Leu Arg Thr Ser Glu Glu Thr Ile Ser	hu_Trail.PRO				
91	Leu Ile Glu Val	Thr Leu Arg Thr Phe Gln Asp Thr Ile Ser	mo_Trail.PRO				
84	Phe Val Arg Lys Met	Ile Leu Lys Thr Tyr Glu Glu Thr Ile Pro	canine_Trail.PRO				
84	Phe Val Arg Lys -	Ile Leu Arg Thr Tyr Glu Glu Thr Ile Pro	feline_Trail.PRO				
		110					
102	Thr Val Gln Glu Lys	Gln Gln Gln Asn Ile Ser Pro Leu Val Arg Glu	hu_Trail.PRO				
106	Thr Val Pro Glu Lys	Gln Leu Ser Thr Pro Pro Leu Pro Arg Gly	mo_Trail.PRO				
99	Thr Ala Pro Glu Lys	Gln Leu Asn Ile Pro Tyr Val Val Ser Asp	canine_Trail.PRO				
98	Thr Val Pro Glu Lys	Gln Leu Asn Ile Pro Tyr Leu Val Arg Glu	feline_Trail.PRO				
		130					
117	Arg Gly Pro Gln Arg	Val Ala Ala His Ile Thr Gly Thr Arg Gly	hu_Trail.PRO				
121	Gly Arg Pro Gln Lys	Val Ala Ala His Ile Thr Gly Ile Thr Arg	mo_Trail.PRO				
114	Arg Gly Ser Gln Arg	Val Ala Ala His Ile Thr Gly Thr Ser Arg	canine_Trail.PRO				
113	Arg Gly Pro Gln Arg	Val Ala Ala His Ile Thr Gly Thr Ser Arg	feline_Trail.PRO				
		140					
132	Arg Ser Asn Thr Leu Ser Ser	Pro Asn Ser Lys Asn Glu Lys Ala	hu_Trail.PRO				
136	Arg Ser Asn Ser Ala Leu	Ile Pro Ile Ser Lys Asp Gly Lys Thr	mo_Trail.PRO				
129	Arg - Ser Met Phe Pro Ile	Pro Ser Lys Asn Asp Lys Ala	canine_Trail.PRO				
128	Arg Arg Ser Thr Phe Pro Val	Pro Ser Lys Asn Glu Lys Ala	feline_Trail.PRO				

FIG. 6C

160																
147	Leu	Gly	Arg	Lys	Ile	Asn	Ser	Trp	Glu	Ser	Ser	Arg	Ser	Gly	His	hu_Trail.PRO
151	Leu	Gly	Gln	Lys	Ile	Glu	Ser	Trp	Glu	Ser	Ser	Arg	Lys	Gly	His	mo_Trail.PRO
143	Leu	Gly	His	Lys	Ile	Asn	Ser	Trp	Asp	Ser	Thr	Arg	Lys	Gly	His	canine_Trail.PRO
143	Leu	Gly	Gln	Lys	Ile	Asn	Ser	Trp	Glu	Ser	Ser	Arg	Lys	Gly	His	feline_Trail.PRO
170																
180																
162	Ser	Phe	Leu	Ser	Asn	Leu	His	Leu	Arg	Asn	Gly	Glu	Leu	Val	Ile	hu_Trail.PRO
166	Ser	Phe	Leu	Asn	His	Val	Leu	Phe	Arg	Asn	Gly	Glu	Leu	Val	Ile	mo_Trail.PRO
158	Ser	Phe	Leu	Asn	Asn	Leu	His	Leu	Arg	Asn	Gly	Glu	Leu	Val	Ile	canine_Trail.PRO
158	Ser	Phe	Leu	Asn	Asn	Leu	His	Leu	Arg	Asn	Gly	Glu	Leu	Val	Ile	feline_Trail.PRO
190																
177	His	Glu	Lys	Gly	Phe	Tyr	Tyr	Ile	Tyr	Ser	Gln	Thr	Tyr	Phe	Arg	hu_Trail.PRO
181	Glu	Gln	Glu	Gly	Leu	Tyr	Tyr	Ile	Tyr	Ser	Gln	Thr	Tyr	Phe	Arg	mo_Trail.PRO
173	His	Gln	Arg	Gly	Phe	Tyr	Tyr	Ile	Tyr	Ser	Gln	Thr	Tyr	Phe	Arg	canine_Trail.PRO
173	His	Gln	Arg	Gly	Phe	Tyr	Tyr	Ile	Tyr	Ser	Gln	Thr	Tyr	Phe	Arg	feline_Trail.PRO
200																
210																
192	Phe	Gln	Glu	-	-	Glu	Ile	Lys	-	-	-	-	Glu	Asn	Thr	hu_Trail.PRO
196	Phe	Gln	Glu	Ala	Glu	Asp	Ala	Ser	Lys	Met	Val	Ser	Lys	Asp	Lys	mo_Trail.PRO
188	Phe	Gln	Glu	Pro	Glu	Glu	Ile	Pro	Thr	-	-	Gly	Gln	Asn	Arg	canine_Trail.PRO
188	Phe	Gln	Glu	Pro	Glu	Glu	Ile	Pro	Thr	-	-	Gly	Gln	Asn	Arg	feline_Trail.PRO
220																
201	Lys	Asn	Asp	Lys	Gln	Met	Val	Gln	Tyr	Ile	Tyr	Lys	Tyr	Thr	Ser	hu_Trail.PRO
211	Val	Arg	Thr	Lys	Gln	Leu	Val	Gln	Tyr	Ile	Tyr	Lys	Tyr	Thr	Ser	mo_Trail.PRO
201	Lys	Arg	Asn	Lys	Gln	Met	Val	Gln	Tyr	Ile	Tyr	Lys	His	Thr	Ser	canine_Trail.PRO
201	Lys	Arg	Asn	Lys	Gln	Met	Val	Gln	Tyr	Ile	Tyr	Lys	His	Thr	Ser	feline_Trail.PRO

FIG. 6D

<hr/>		230	240
216	Tyr Pro Asp Pro Ile Leu Leu Met Lys Ser Ala Arg Asn Ser Cys		hu_Trail.PRO
226	Tyr Pro Asp Pro Ile Val Leu Met Lys Ser Ala Arg Asn Ser Cys		mo_Trail.PRO
216	Tyr Pro Asp Pro Ile Leu Leu Met Lys Ser Ala Arg Asn Ser Cys		canine_Trail.PRO
216	Tyr Pro Asp Pro Ile Leu Leu Met Lys Ser Ala Arg Asn Ser Cys		feline_Trail.PRO
<hr/>		250	
231	Trp Ser Lys Asp Ala Glu Tyr Gly Leu Tyr Ser Ile Tyr Gln Gly		hu_Trail.PRO
241	Trp Ser Arg Asp Ala Glu Tyr Gly Leu Tyr Ser Ile Tyr Gln Gly		mo_Trail.PRO
231	Trp Ser Lys Asp Ser Glu Tyr Gly Leu Tyr Ser Ile Tyr Gln Gly		canine_Trail.PRO
231	Trp Ser Lys Asp Ser Glu Tyr Gly Leu Tyr Ser Ile Tyr Gln Gly		feline_Trail.PRO
<hr/>		260	270
246	Gly Ile Phe Glu Leu Lys Lys Glu Asn Asp Arg Ile Phe Val Ser Val		hu_Trail.PRO
256	Gly Leu Phe Glu Leu Lys Lys Asn Asp Arg Ile Phe Val Ser Val		mo_Trail.PRO
246	Gly Ile Phe Glu Leu Lys Glu Asn Asp Arg Ile Phe Val Ser Val		canine_Trail.PRO
246	Gly Ile Phe Glu Leu Lys Glu Asn Asp Arg Ile Phe Val Ser Val		feline_Trail.PRO
<hr/>		280	
261	Thr Asn Glu His Leu Ile Asp Met Asp His Glu Ala Ser Phe Phe		hu_Trail.PRO
271	Thr Asn Glu His Leu Met Asp Leu Asp Gln Glu Ala Ser Phe Phe		mo_Trail.PRO
261	Ser Asn Glu Gln Leu Ile Asp Met Asp Gln Glu Ala Ser Phe Phe		canine_Trail.PRO
261	Ser Asn Glu Gln Leu Ile Asp Met Asp Gln Glu Ala Ser Phe Phe		feline_Trail.PRO
<hr/>		290	
276	Gly Ala Phe Leu Val Gly ter		hu_Trail.PRO
286	Gly Ala Phe Leu Ile Asn ter		mo_Trail.PRO
276	Gly Ala Phe Leu Ile Gly ter		canine_Trail.PRO
276	Gly Ala Phe Leu Ile Gly ter		feline_Trail.PRO

FIG. 7A

V R E R G P Q R V A A H I T G T S R R S S T F P I P S S K N E K A L G Q K I N S										Majority
10 20 30 40										
1	V	R	E	R	G	P	Q	R	V	hu_Trail_sh.PRO
1	P	R	G	G	R	P	Q	K	V	mo_Trail_sh.PRO
1	V	S	D	R	G	S	Q	R	V	canine_Trail_sh.PRO
1	V	R	E	R	G	P	Q	R	V	feline_Trail2_sh.PRO
W E S S R K G H S F L N N L H L R N G E L V I H Q R G F Y Y I Y S Q T Y F R F Q										Majority
50 60 70 80										
41	W	E	S	S	R	S	G	H	S	hu_Trail_sh.PRO
41	W	E	S	S	R	K	G	H	S	mo_Trail_sh.PRO
40	W	D	S	S	T	R	K	G	H	canine_Trail_sh.PRO
41	W	E	S	S	R	K	G	H	S	feline_Trail2_sh.PRO
E P E E I P T - - G Q N R K R N K Q M V Q Y I Y K H T S Y P D P I L L M K S A R										Majority
90 100 110 120										
81	E	-	-	E	I	K	-	-	-	hu_Trail_sh.PRO
81	E	A	E	D	A	S	K	M	V	mo_Trail_sh.PRO
80	E	P	E	E	I	P	T	-	-	canine_Trail_sh.PRO
81	E	P	E	E	I	P	T	-	-	feline_Trail2_sh.PRO

FIG. 7B

NSCWSKDAEYGLYSIYQGGIFFELKENDRIFVSVSNELLID													Majority
													160

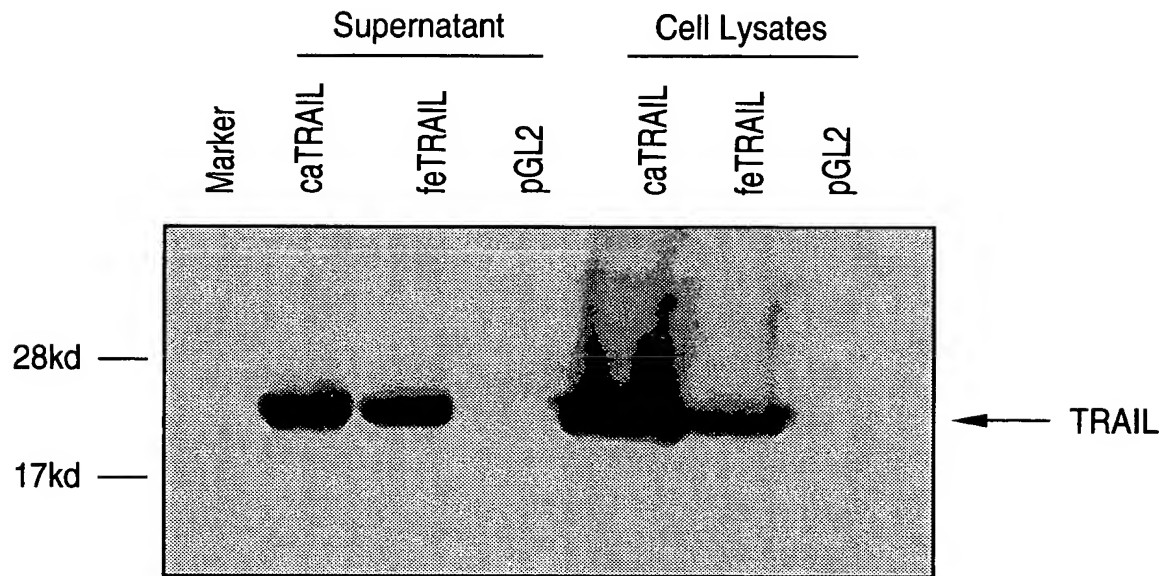
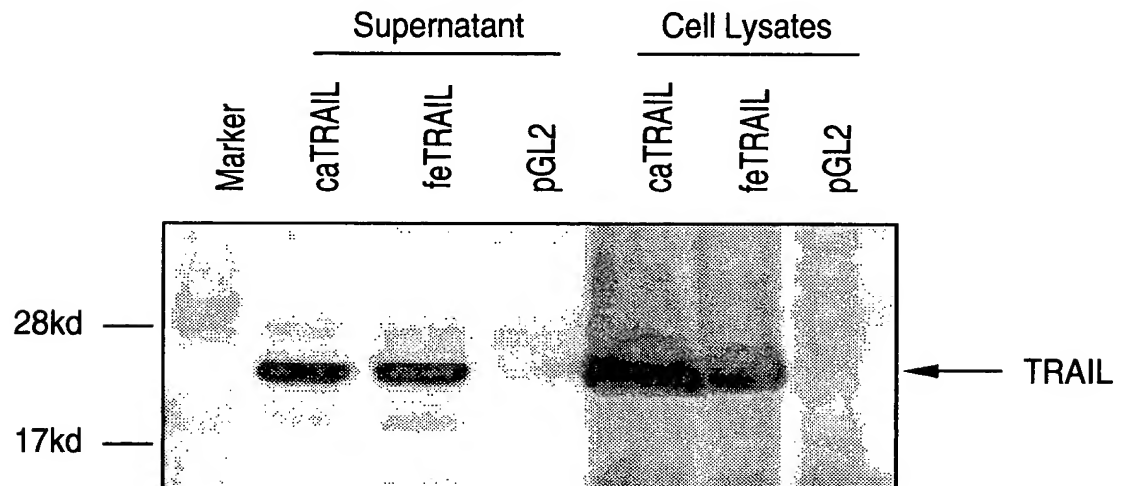
FIG. 8A**FIG. 8B**

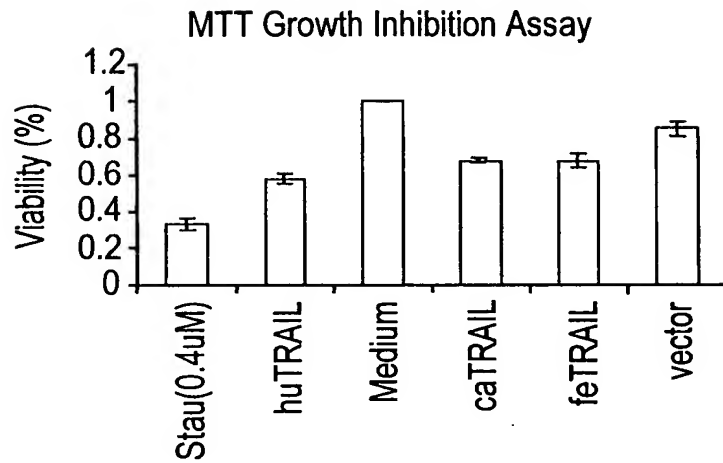
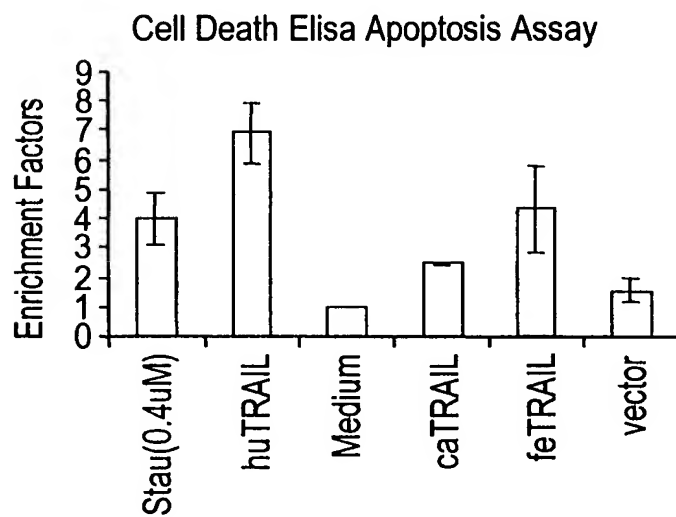
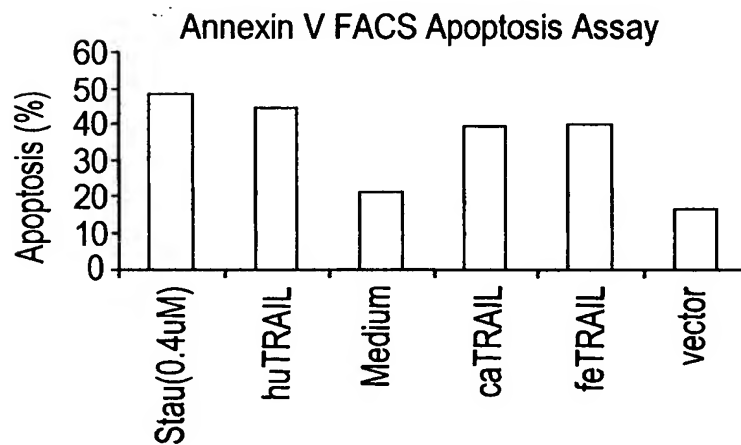
FIG. 9A**FIG. 9B****FIG. 9C**

FIG. 10A

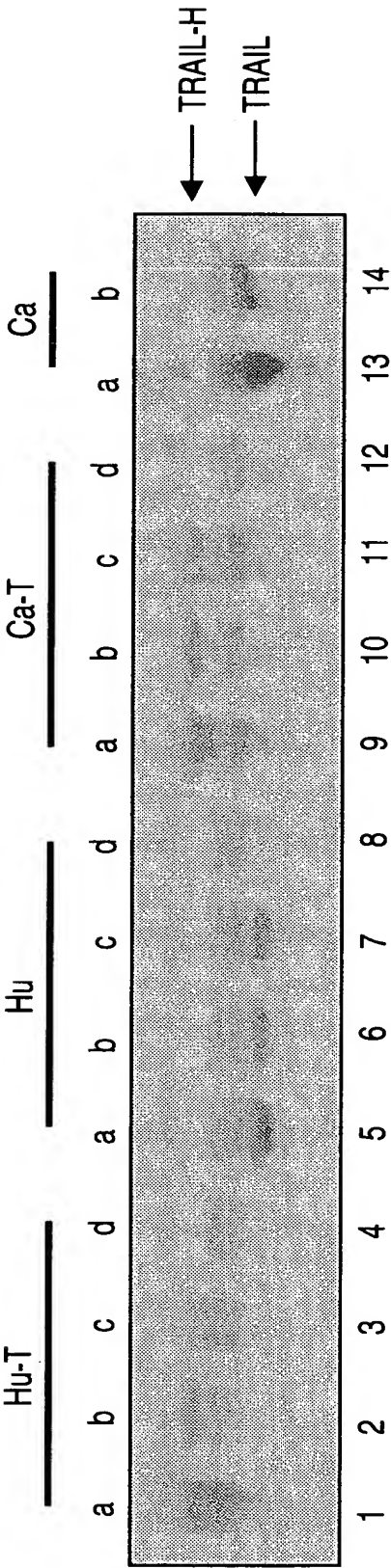


FIG. 10B

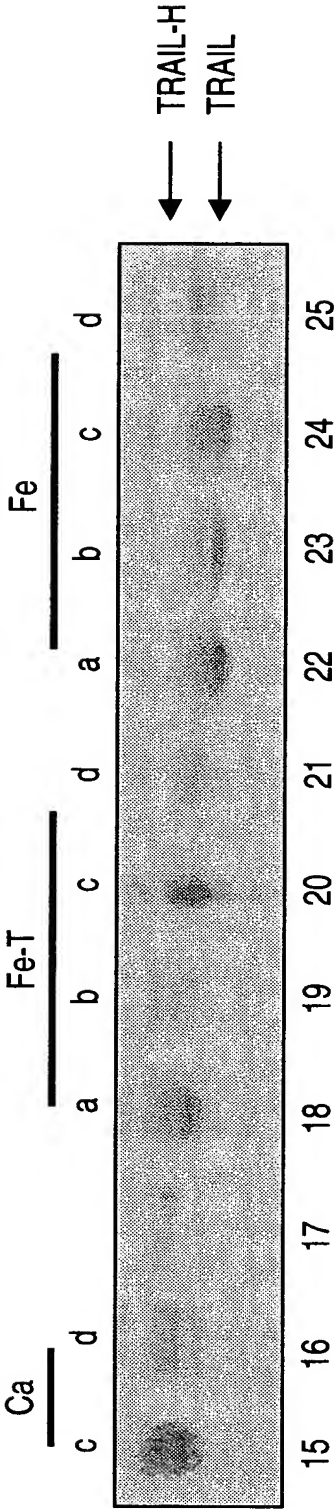


FIG. 11A

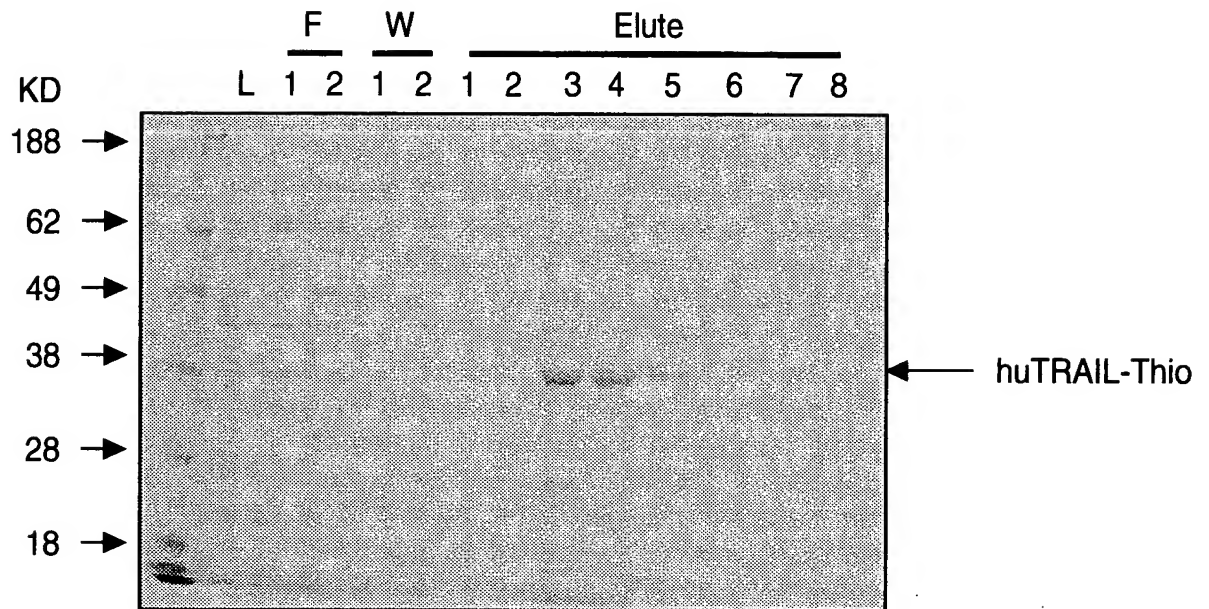


FIG. 11B

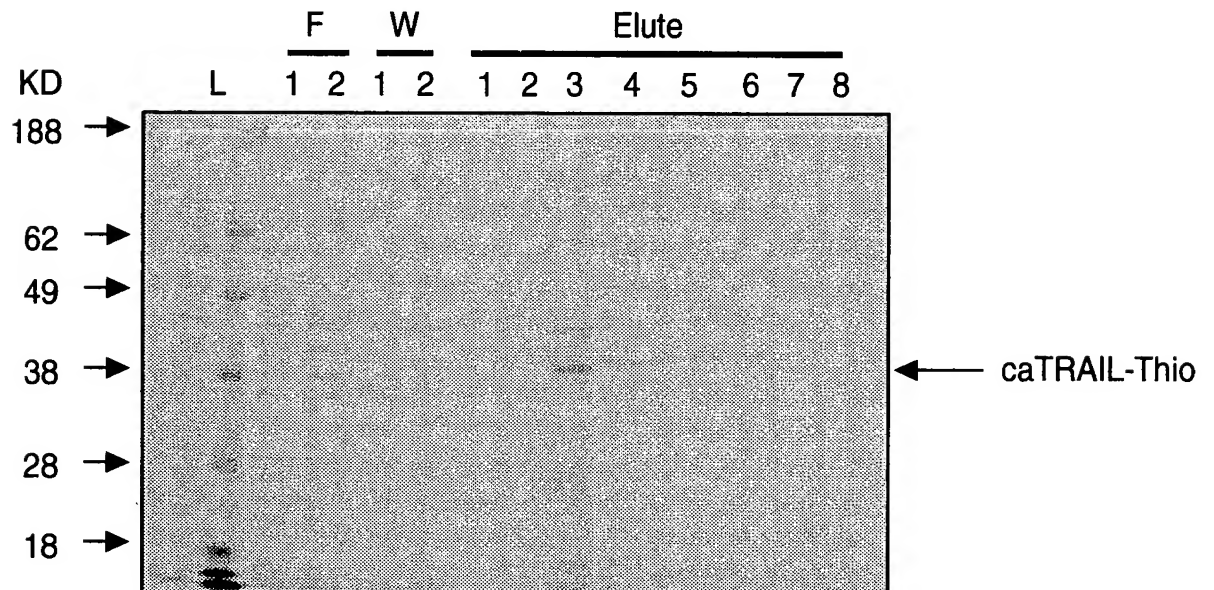


FIG. 12

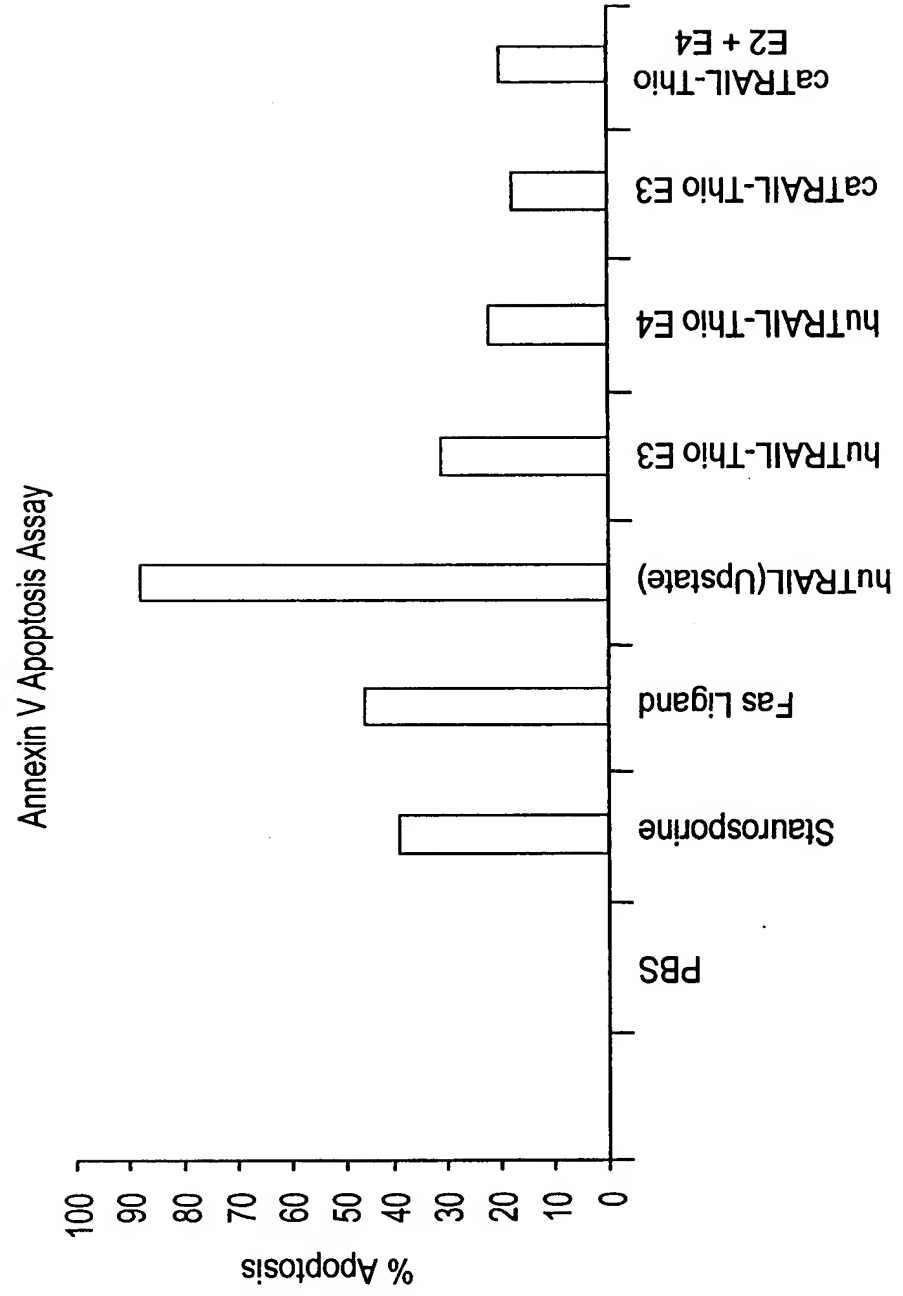


FIG. 13A

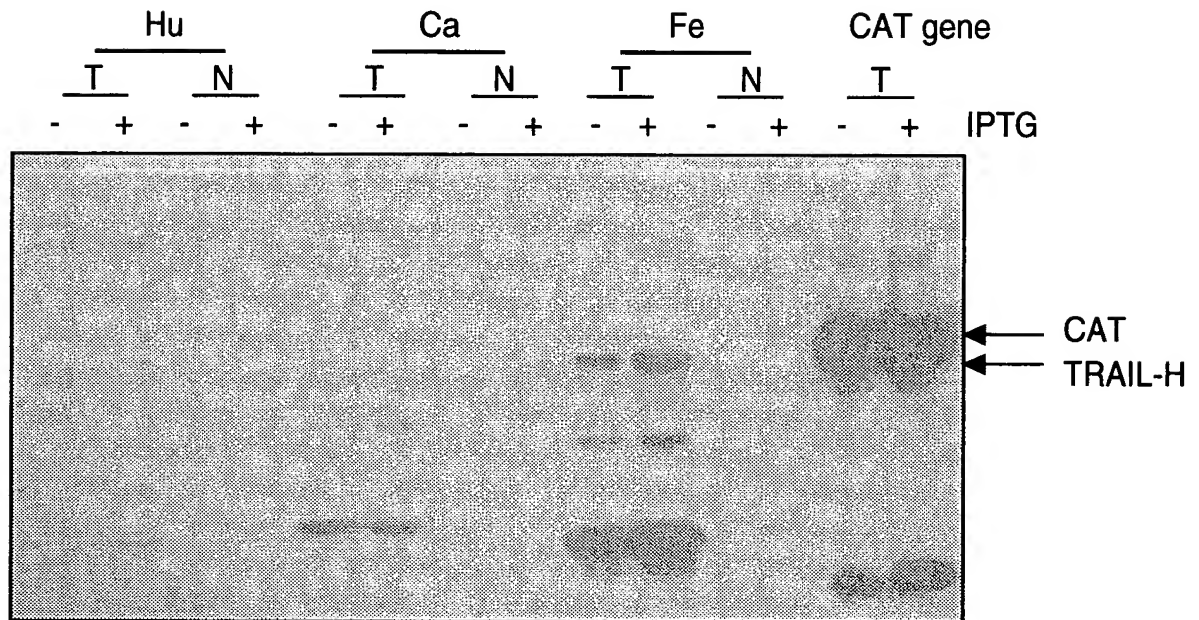


FIG. 13B

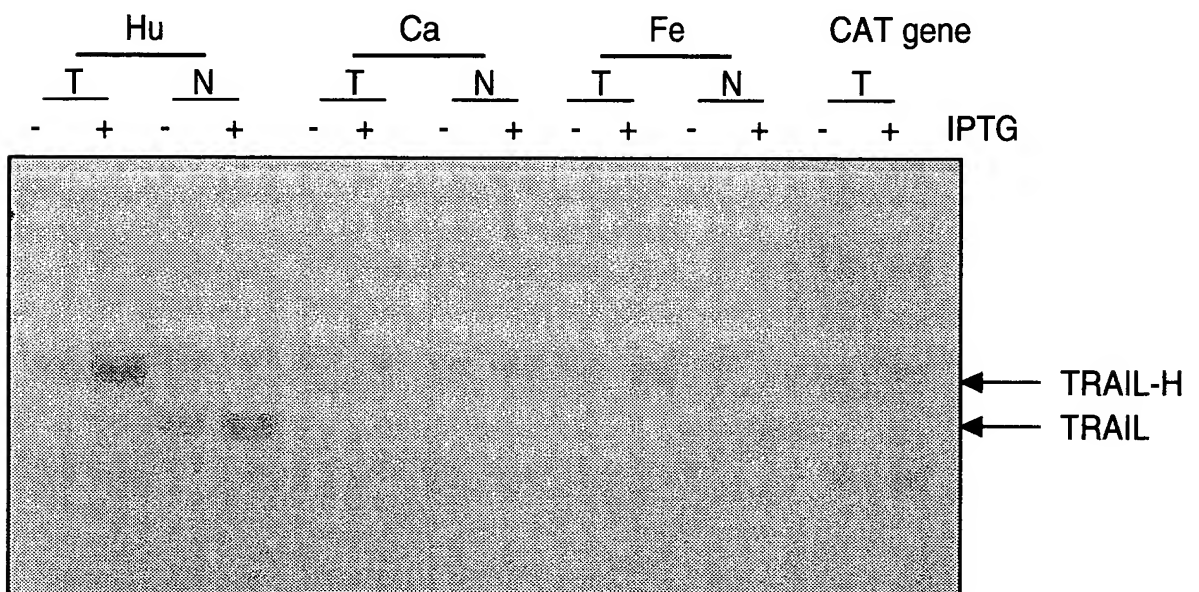


FIG. 14A

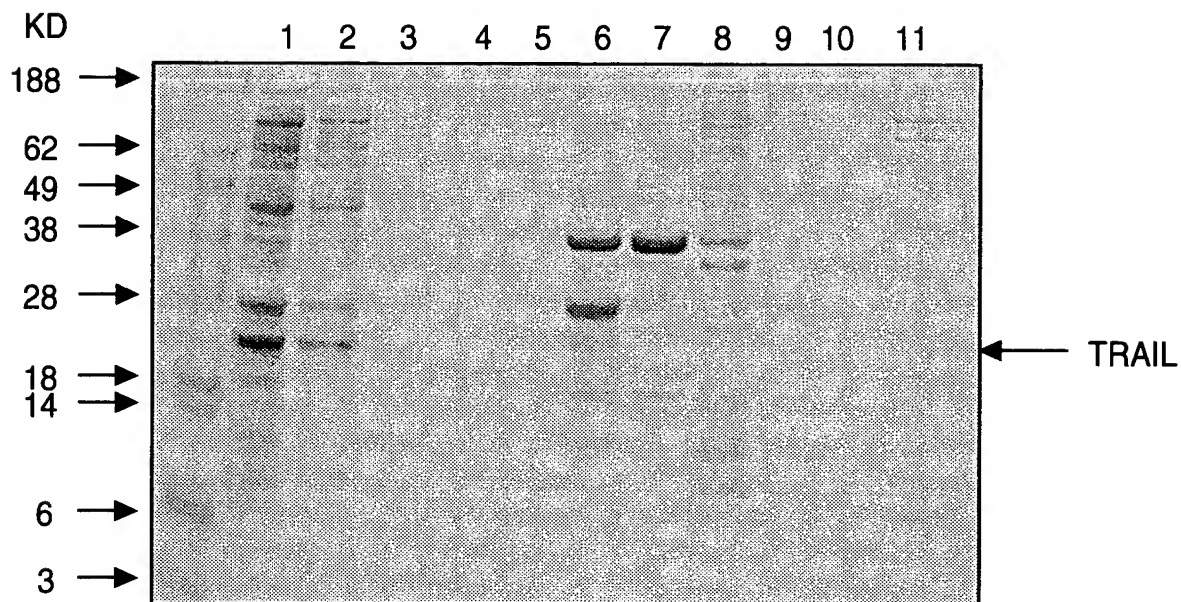


FIG. 14B

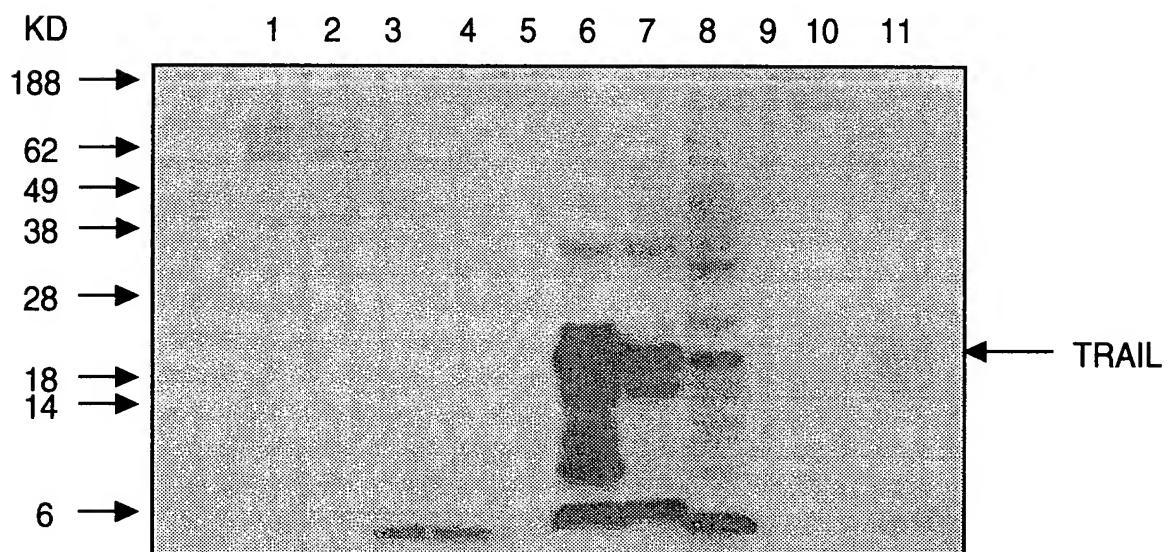


FIG. 15A

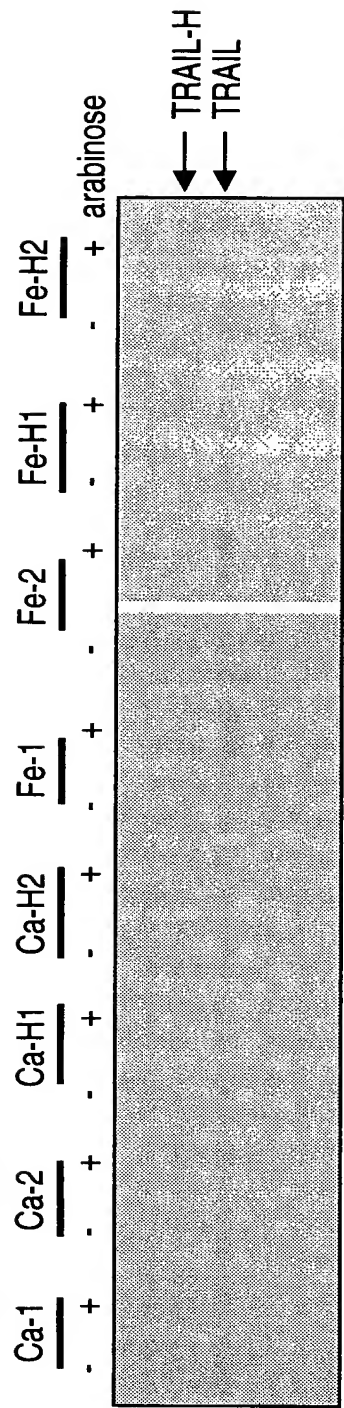


FIG. 15B

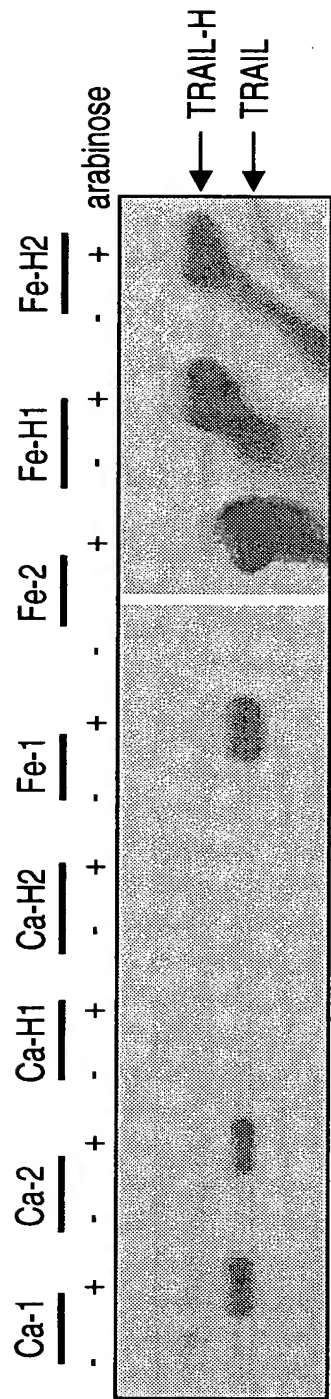


FIG. 15C

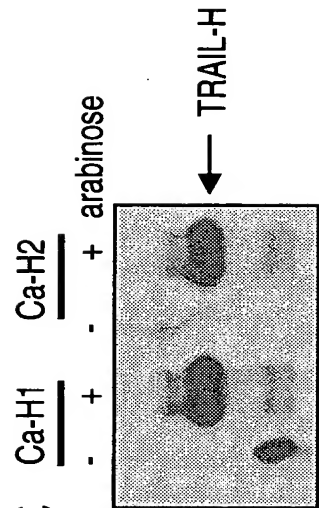


FIG. 16A

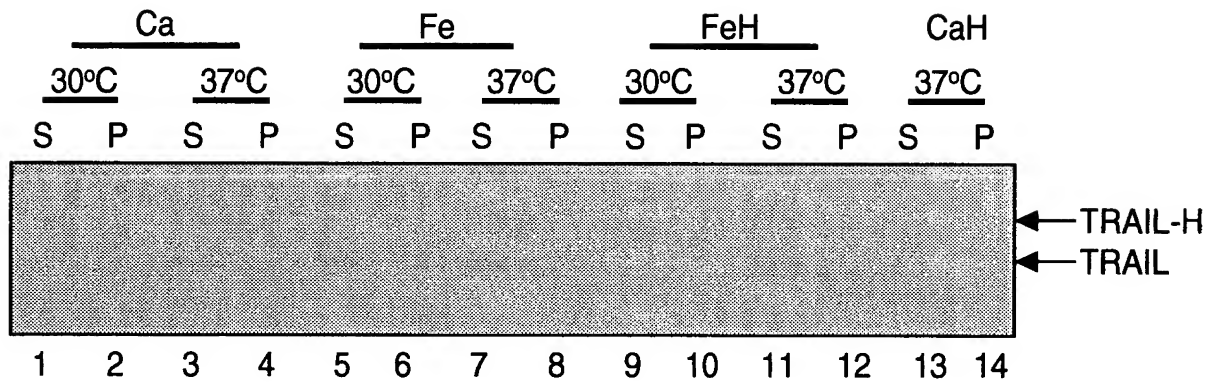


FIG. 16B

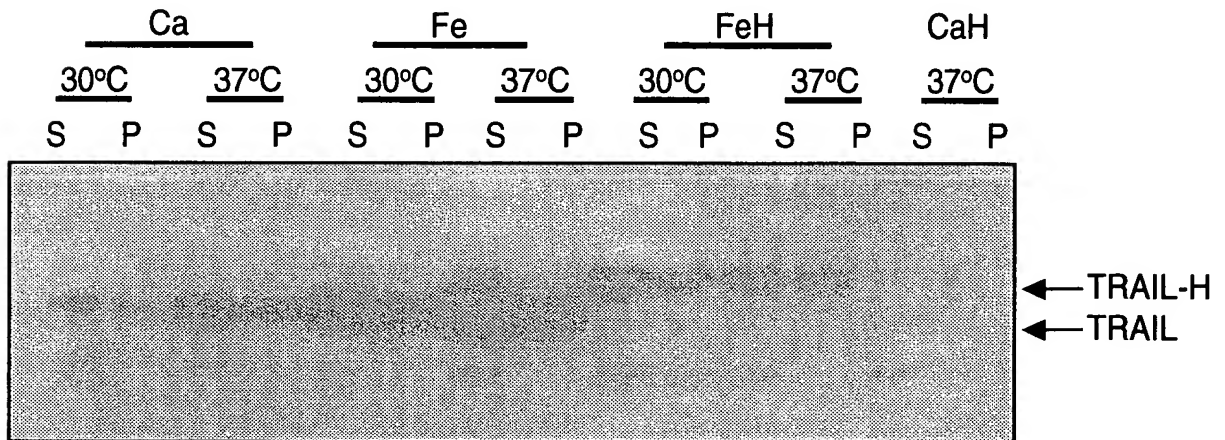


FIG. 17A

Elute

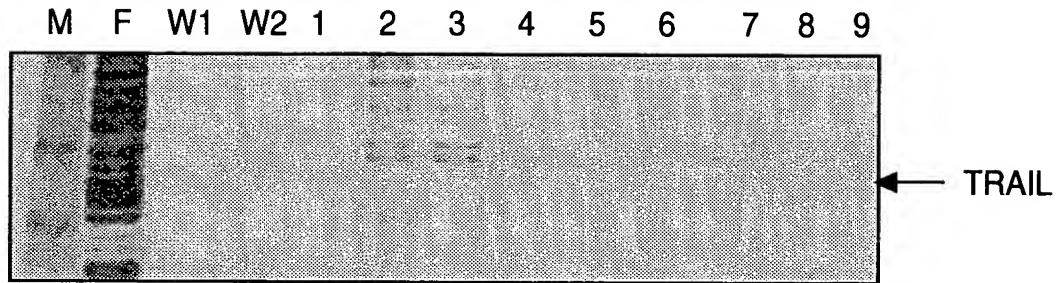


FIG. 17B

Elute

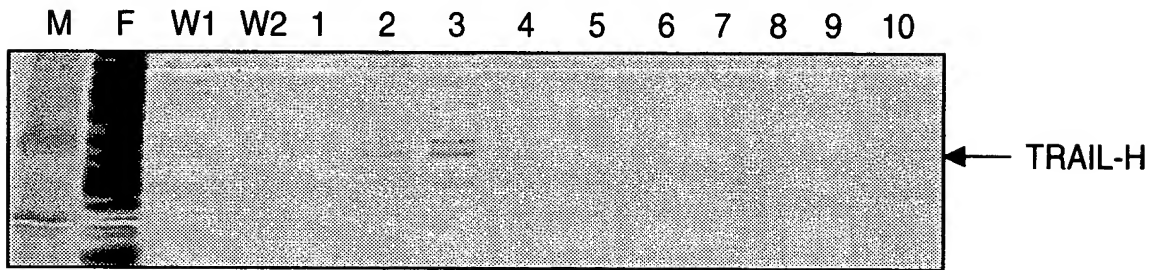


FIG. 17C

Elute

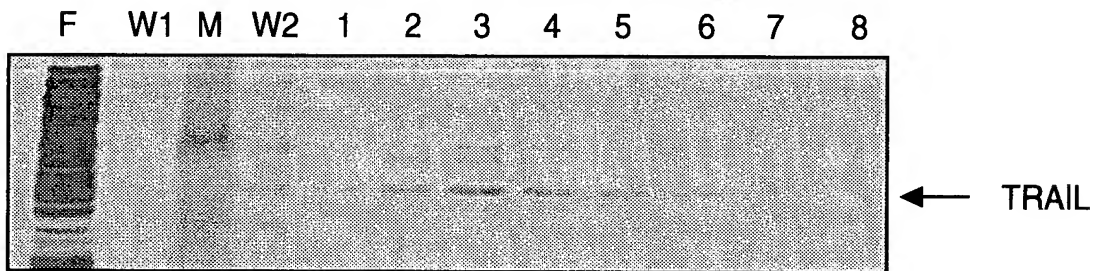
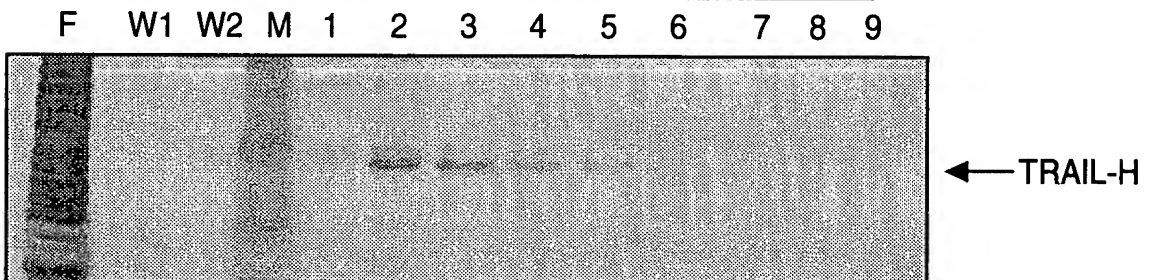


FIG. 17D

Elute



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FIG. 17E

Elute

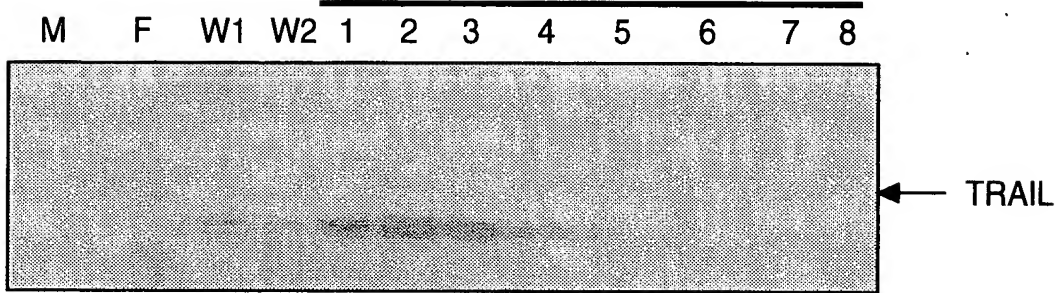


FIG. 17F

Elute

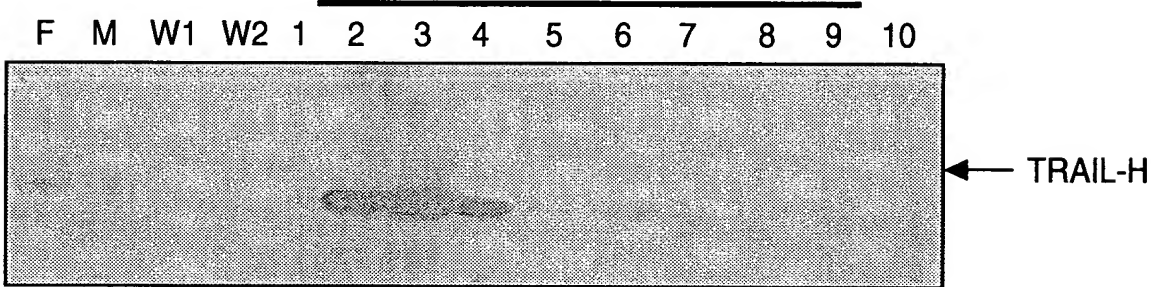


FIG. 17G

Elute

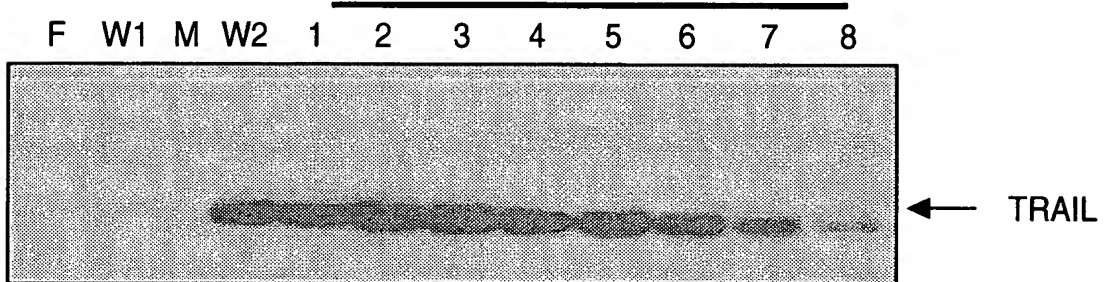
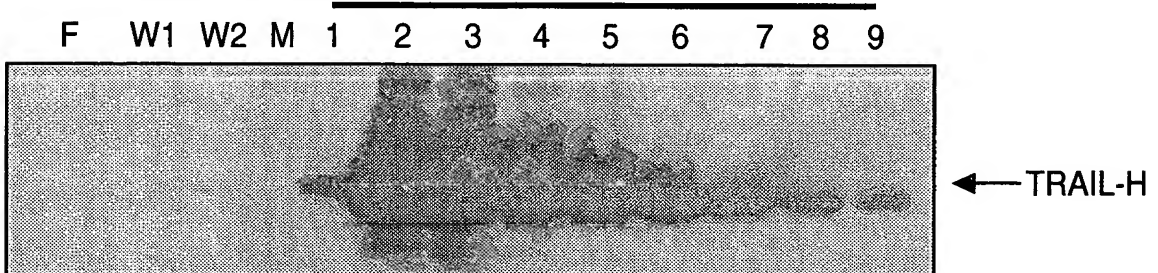


FIG. 17H

Elute



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FIG. 18A

MTT Growth inhibition Assay

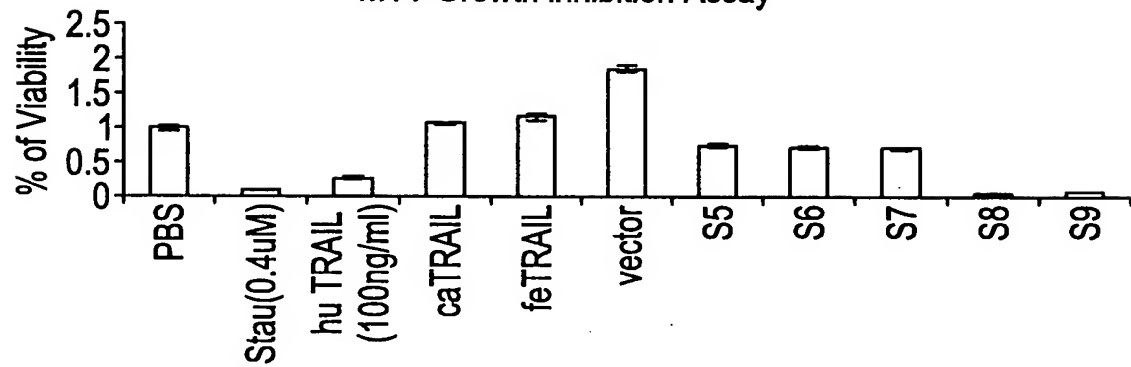


FIG. 18B

Cell Death Elisa Apoptosis Assay

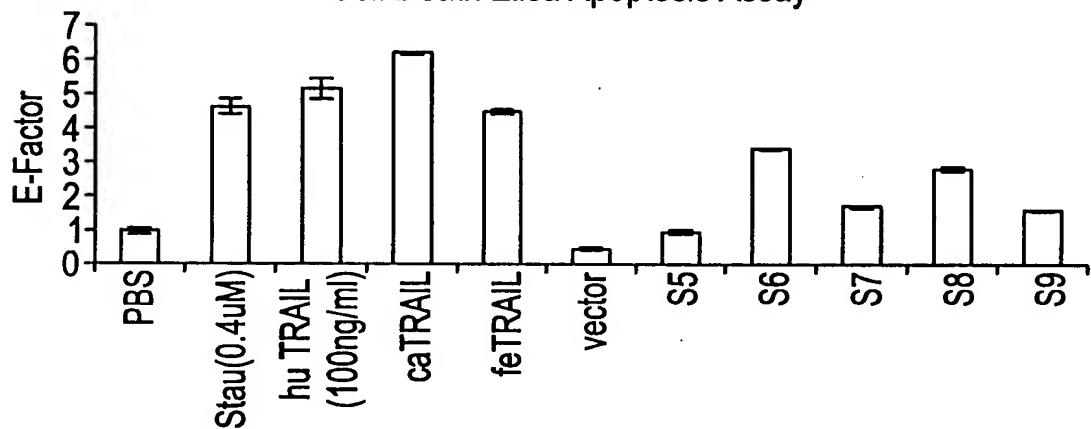


FIG. 18C

Annexin V FITC Apoptosis Assay

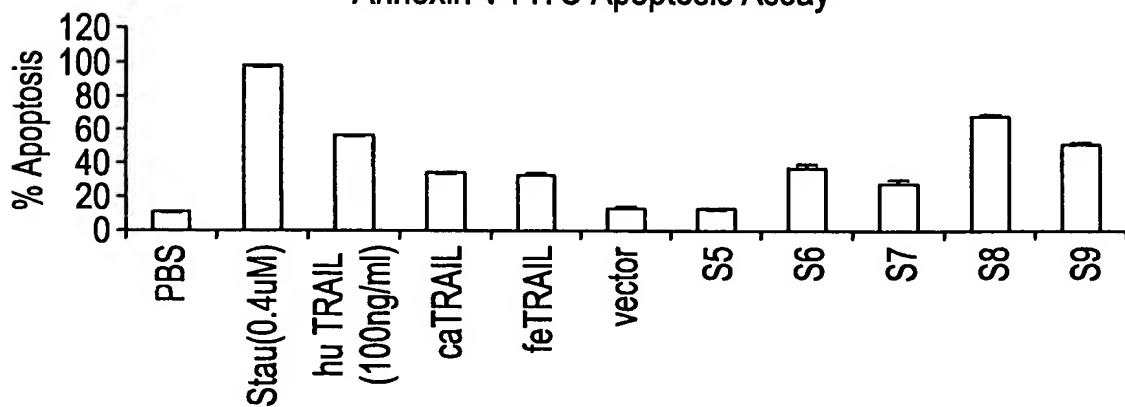


FIG. 19A

MTT Growth Inhibition Assay

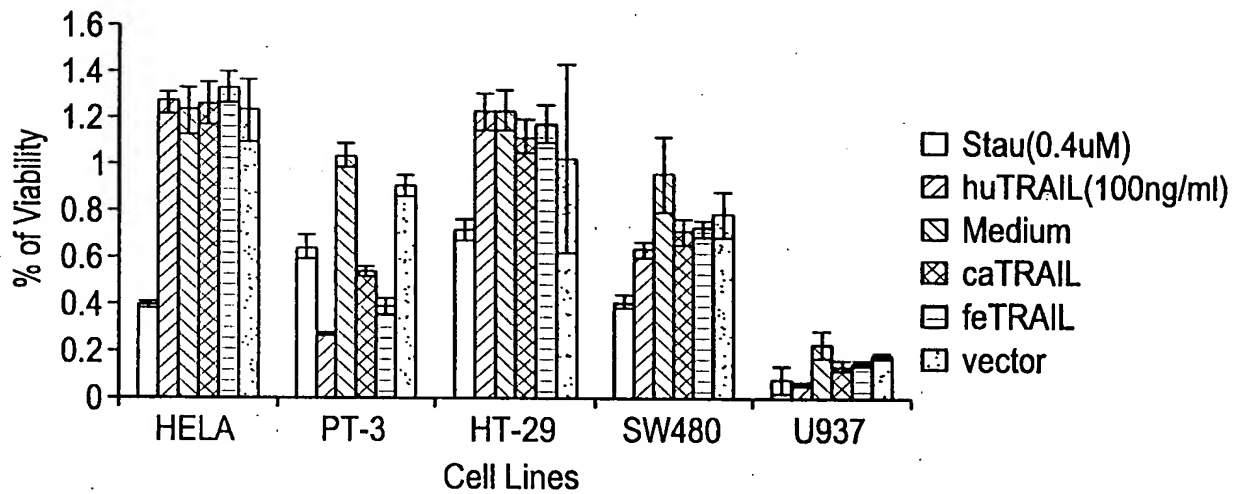


FIG. 19B

Cell Death Elisa Apoptosis Assay

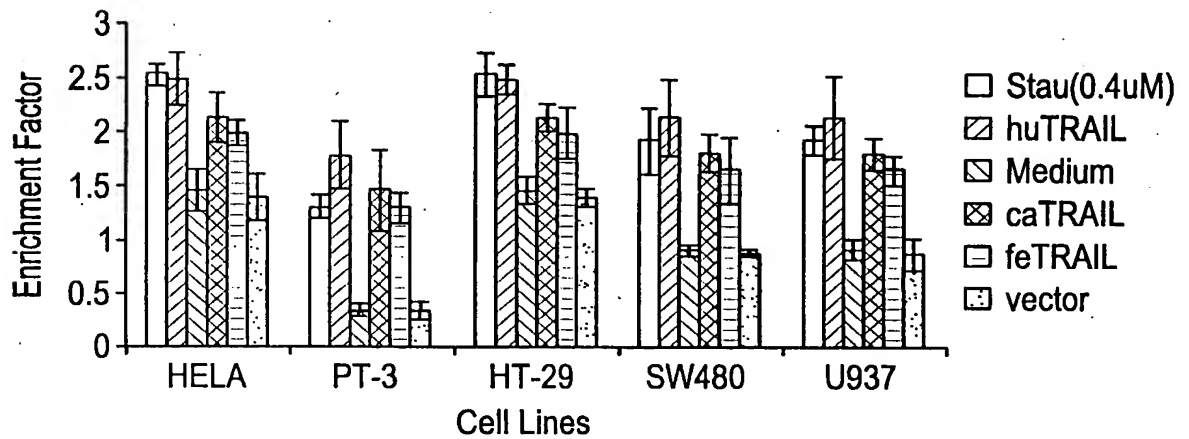


FIG. 20A

MTT Growth Inhibition Assay for Canine
Cell Lines

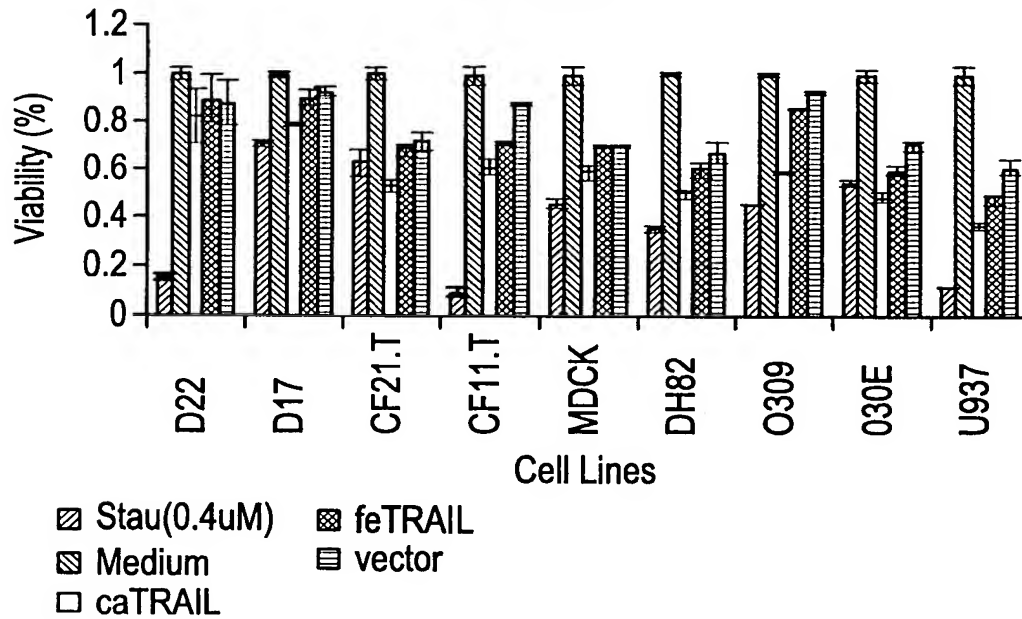


FIG. 20B

Cell Death Elisa Apoptosis Assay for Canine Cell Lines

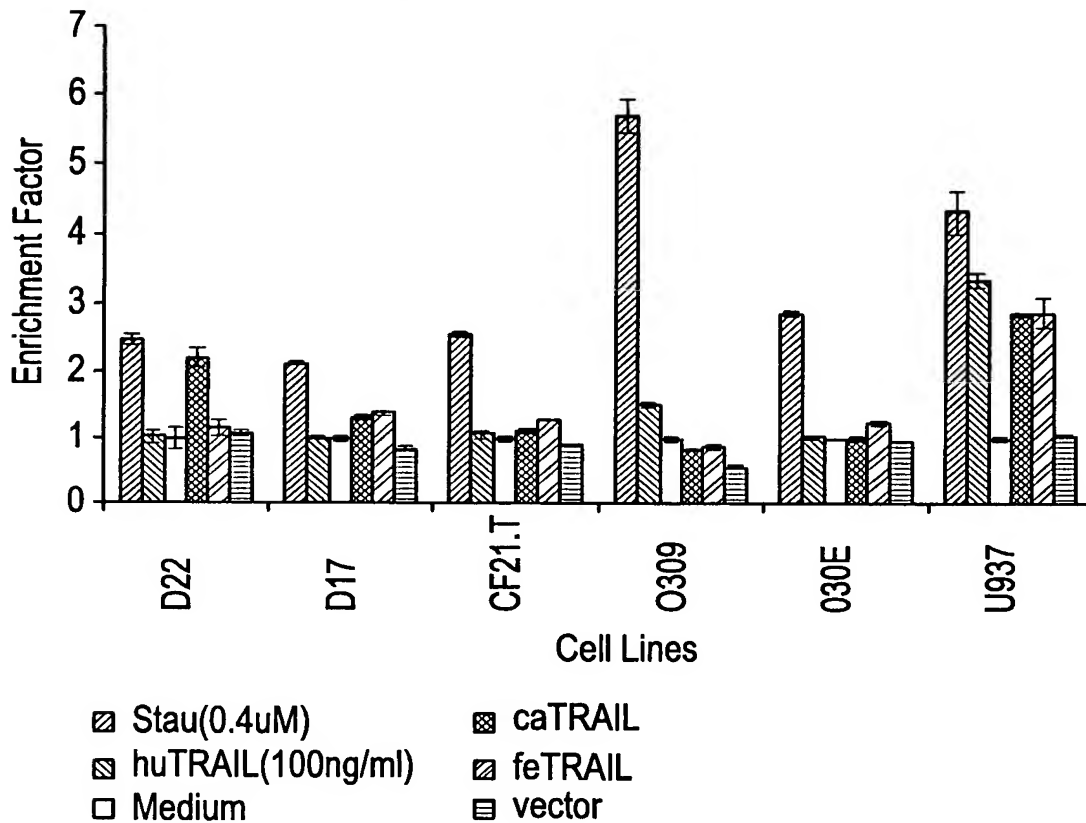


FIG. 21A

MTT Growth Inhibition Assay

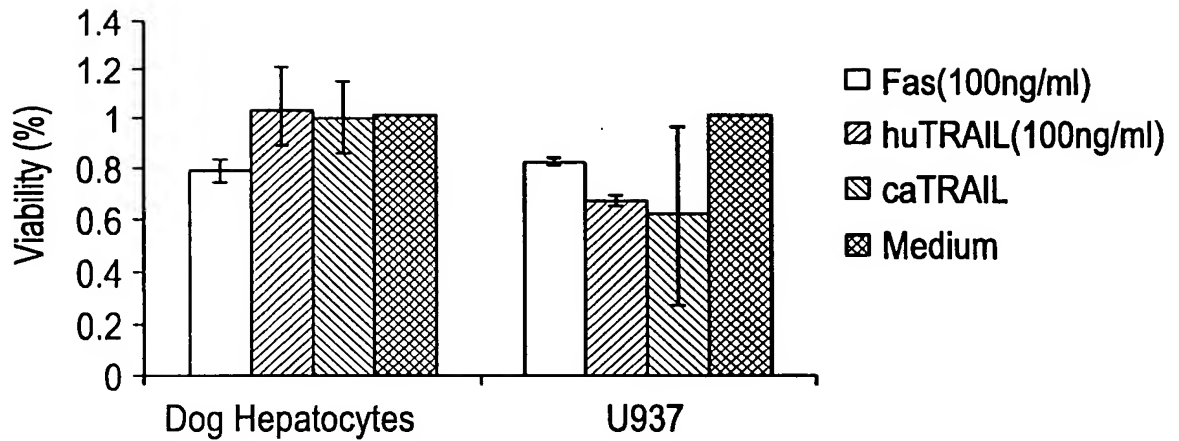


FIG. 21B

Cell Death Elisa Apoptosis Assay

